

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: SHANNON POLEY Examiner #: 77851 Date: 2/3/00
 Art Unit: 1648 Phone Number 308 3783 Serial Number: 09/612569
 Mail Box and Bldg/Room Location: 8612/8619 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Maternal computers and methods

Inventors (please provide full names): Peter ROELVINK; Joseph CRUPER; Jane KQUES DI;
Thomas J. WICKHAM

Earliest Priority Filing Date: 2/9/00

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please include an inventor name search.

Phase search for a complex comprising a virus (empty) (empty or satires) that has viral capsid proteins within it. The complex has a non-native ligand that recognized an epitope on an immune effector cell (MHC I + for II) and a nucleic acid that encodes a non-native antigen.

The ligand recognizes lysine or histidine residues.

The complex also has a liposome, lipid bilayers, ligand D26,600.480

The virus is non-enveloped + has an adenovirus capsid.

All of this is in a pharmaceutical composition.

epitope D24,611.216.550 antibody (a) anti-idiotypic antibody affinity epitope mapping molecular mapping antigen (a) (electronic) (spec?)

capsid B34,950.500.320 B12,776.914.700.250 capsid protein coat protein viral coat protein

radioligand assay receptors (a) cell surface

virion B34,950.500.320 B12,776.914.700.250 virus particles

Phase give to Mary Hale.

Claims 1-32 + 40-43 only.

STAFF USE ONLY

Searcher: Mary
 Searcher Phone #: _____

Type of Search

NA Sequence (#) _____

Vendors and cost where applicable

STN 125.24

Searcher Location: _____

Structure (#) _____

Questel/Orbit _____

Date Searcher Picked Up: _____

Bibliographic _____

Dr.Link _____

Date Completed: 2/9

Litigation _____

Lexis/Nexis _____

Searcher Prep & Review Time: 14

Fulltext _____

Sequence Systems _____

Clerical Prep Time: _____

Patent Family _____

WWW/Internet _____

Online Time: 9

Other _____

Other (specify) _____

70ley
617569

=> fil medl,caplus,biosis,embase,wpids,jicst

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'MEDLINE' ENTERED AT 10:10:03 ON 09 FEB 2001

FILE 'CAPLUS' ENTERED AT 10:10:03 ON 09 FEB 2001
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=> s (virion or b4.950/ct or virus particle) and (capsid or b4.950.500.250/ct or d12.776.964.970.600.250/ct or capsid protein or coat? protein or viral coat? protein)

L1	2813	FILE MEDLINE
L2	3096	FILE CAPLUS
L3	2645	FILE BIOSIS
L4	2343	FILE EMBASE
L5	77	FILE WPIDS
L6	130	FILE JICST-EPLUS

TOTAL FOR ALL FILES

L7 11104 (VIRION OR B4.950/CT OR VIRUS PARTICLE) AND (CAPSID OR B4.950.500.250/CT OR D12.776.964.970.600.250/CT OR CAPSID PROTEIN OR COAT? PROTEIN OR VIRAL COAT? PROTEIN)

=> s l7 and (liposome or lipid bilayer! or ligand or d26.600.480/ct or radioligand assay or receptor!(a)cell surface)

L8	52	FILE MEDLINE
L9	64	FILE CAPLUS
L10	31	FILE BIOSIS
L11	43	FILE EMBASE
L12	3	FILE WPIDS
L13	1	FILE JICST-EPLUS

TOTAL FOR ALL FILES

L14 194 L7 AND (LIPOosome OR LIPID BILAYER! OR LIGAND OR D26.600.480/CT OR RADIOligand ASSAY OR RECEPTOR!(A) CELL SURFACE)

=> s l14 and (epitope or d24.611.216.550/ct or antibod?(a)anti idiotyp? or
antibod? affinity? or epitope map? or molecular mimicry or
antigen(w)(determin? or specif?))

L15 7 FILE MEDLINE
L16 11 FILE CAPLUS
L17 4 FILE BIOSIS
L18 5 FILE EMBASE
L19 0 FILE WPIDS
L20 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L21 27 L14 AND (EPITOPE OR D24.611.216.550/CT OR ANTIBOD?(A) ANTI
IDIOT
YP? OR ANTIBOD? AFFINITY? OR EPITOPE MAP? OR MOLECULAR MIMICRY
OR ANTIGEN(W) (DETERMIN? OR SPECIF?))

=> s l21 and (mhc(w)(i or ii) or (g4.610.626.580.595 or g5.511.580.595 or
g5.275.364 or g4.610.626.580.600 or g5.275.370 or g5.511.580.600)/ct)

L22 0 FILE MEDLINE
L23 0 FILE CAPLUS
L24 0 FILE BIOSIS
L25 0 FILE EMBASE
L26 0 FILE WPIDS
L27 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L28 0 L21 AND (MHC(W) (I OR II) OR (G4.610.626.580.595 OR
G5.511.580.59
5 OR G5.275.364 OR G4.610.626.580.600 OR G5.275.370 OR
G5.511.58
0.600)/CT)

=> s l21 and cd40

L29 0 FILE MEDLINE
L30 1 FILE CAPLUS
L31 0 FILE BIOSIS
L32 0 FILE EMBASE
L33 0 FILE WPIDS
L34 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L35 1 L21 AND CD40

=> s l21 and rgd motif

L36 0 FILE MEDLINE
L37 0 FILE CAPLUS
L38 0 FILE BIOSIS
L39 0 FILE EMBASE
L40 0 FILE WPIDS
L41 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L42 0 L21 AND RGD MOTIF

=> s rgd and l21

L43 1 FILE MEDLINE

L44 1 FILE CAPLUS

L45 1 FILE BIOSIS

L46 1 FILE EMBASE

L47 0 FILE WPIDS

L48 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L49 4 RGD AND L21

=> d l35 cbib abs;s l49 not l35

L35 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS

1996:676262 Document No. 125:319219 Immunology of gene therapy with
adenoviral vectors in mouse skeletal muscle. Yang, Yiping; Haecker,
Sarah

Ehlen; Su, Qin; Wilson, James M. (Inst. for Human Gene Therapy, Univ.
Pennsylvania Medical Center and Wistar Inst., Philadelphia, PA, 19104,
USA). Hum. Mol. Genet., 5(11), 1703-1712 (English) 1996. CODEN: HMGEE5.
ISSN: 0964-6906.

AB Skeletal muscle is an attractive target for somatic gene transfer of both
acquired and inherited disorders. Direct injection of adenoviral vectors
in the skeletal muscle leads to recombinant gene expression in a large

no.

of muscle fibers. Transgene expression has been transient in most organs
and assocd. with substantial inflammation when expts. are performed in
adult immune competent mice. In this report, we utilize a variety of in
vivo and in vitro models of T and B cell function to characterize the
nature of the immune response to adenoviral vectors injected into murine
skeletal muscle. Cellular immunity dependent on CD4+ and CD8+ T cells
contributes to the loss of recombinant gene expression and the

development

of localized inflammation. **Antigen specific**

activation of T cells occurs to both viral proteins and the reporter gene
.beta.-galactosidase. Systemic levels of neutralizing antibody to the
capsid proteins of the vector are also generated.

Destructive immune responses responsible for loss of transgene expression
are largely directed against .beta.-galactosidase in that transgene
expression was stable when .beta.-galactosidase was eliminated as a
neoantigen in mice transgenic for lacZ. A strategy to prevent the
cellular and humoral immunity to this therapy was developed based on
transiently ablating CD4+ T cell activation at the time of vector
delivery. Encouraging results were obtained when vector was administered
with one of several immune modulating agents including cyclophosphamide,
mAb to CD4+ cells, and mAb to **CD40 ligand**. These
studies indicate that cellular and humoral immune responses are elicited
in the context of gene therapy directed to skeletal muscle with

adenoviral

vectors. Transient ablation of CD4+ T cell activation prevents the
effector responses of the CD8+ T and B cells.

L50 1 FILE MEDLINE
 L51 1 FILE CAPLUS
 L52 1 FILE BIOSIS
 L53 1 FILE EMBASE
 L54 0 FILE WPIDS
 L55 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L56 4 L49 NOT L35

=> dup rem l56

PROCESSING COMPLETED FOR L56

L57 1 DUP REM L56 (3 DUPLICATES REMOVED)

=> d cbib abs

L57 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
 1998443237 Document Number: 98443237. Conformational flexibility in a highly mobile protein loop of foot-and-mouth disease virus: distinct structural requirements for integrin and antibody binding. Feliu J X; Benito A; Oliva B; Aviles F X; Villaverde A. (Institut de Biologia Fonamental, Universitat Aut`onoma de Barcelona Bellaterra, 08193 Barcelona Spain.) JOURNAL OF MOLECULAR BIOLOGY, (1998 Oct 23) 283 (2) 331-8. Journal code: J6V. ISSN: 0022-2836. Pub. country: ENGLAND: United Kingdom. Language: English.
 AB The G-H loop of foot-and-mouth disease virus VP1 protein is a highly mobile peptide, that extends from the **capsid** surface and that in native **virions** is invisible by X-ray crystallography. In serotype C, this segment contains a hypervariable region with several continuous, overlapping, B-cell **epitopes** that embrace the conserved Arg-Gly-Asp (**RGD**) cell attachment motif. The solvent-exposed positioning of this peptide by selective insertion into different structural frameworks of E. coli beta-galactosidase, generates a spectrum of antigenic variants which react distinctively with a panel of anti-VP1 monoclonal antibodies and exhibit different efficiencies as cell **ligands**. The cell attachment efficiency is much less restricted by the different positioning of the viral segment at the insertion sites. A molecular model of an inserted stretch reveals a highest flexibility of the **RGD** tripeptide segment compared with the flanking sequences, that could allow a proper accommodation to integrin receptors even in poorly antigenic conformations. The non-converging structural requirements for **RGD**-mediated integrin binding and antibody recognition, explains the dynamism of the generation of neutralisation-resistant antigenic variants in the viral quasi-species, arising from a conformational space of integrin-binding competent peptides. This might be of special relevance for foot-and-moth disease virus evolution, since unlike in other picornaviruses, the cell binding motif and the major

neutralising B-cell **epitopes** overlap in a solvent-exposed peptide accessible to the host immune system, in a **virion** lacking canyons and similar hiding structures. Copyright 1998 Academic Press.

=> s roelvink p?/au,in;s bruder j?/au,in;s kovesdi i?/au,in;s wickham t?/au,in

'IN' IS NOT A VALID FIELD CODE
L58 16 FILE MEDLINE
L59 29 FILE CAPLUS
L60 28 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L61 15 FILE EMBASE
L62 7 FILE WPIDS
L63 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L64 95 ROELVINK P?/AU,IN

'IN' IS NOT A VALID FIELD CODE
L65 47 FILE MEDLINE
L66 56 FILE CAPLUS
L67 62 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L68 46 FILE EMBASE
L69 25 FILE WPIDS
L70 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L71 236 BRUDER J?/AU,IN

'IN' IS NOT A VALID FIELD CODE
L72 93 FILE MEDLINE
L73 140 FILE CAPLUS
L74 124 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L75 88 FILE EMBASE
L76 24 FILE WPIDS
L77 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L78 469 KOVESDI I?/AU,IN

'IN' IS NOT A VALID FIELD CODE
L79 41 FILE MEDLINE
L80 56 FILE CAPLUS
L81 57 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L82 37 FILE EMBASE
L83 16 FILE WPIDS
L84 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L85 207 WICKHAM T?/AU, IN

=> s 164 and 171 and 178 and 185

L86 0 FILE MEDLINE
L87 3 FILE CAPLUS
L88 0 FILE BIOSIS
L89 0 FILE EMBASE
L90 3 FILE WPIDS
L91 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES

L92 6 L64 AND L71 AND L78 AND L85

=> dup rem 192

PROCESSING COMPLETED FOR L92

L93 3 DUP REM L92 (3 DUPLICATES REMOVED)

=> d cbib abs 1-3

L93 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1

2000:191242 Document No. 132:232728 Adenovirus having a modified fiber protein leading to reduced targeting for the native adenoviral receptor. Wickham, Thomas J.; Kovesdi, Imre; Roelvink, Petrus W.; Bruder, Joseph T. (Genvec, Inc., USA). PCT Int. Appl. WO 2000015823 A1 20000323, 69 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR,

BY,

CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG.

(English). CODEN: PIXXD2. APPLICATION: WO 1999-US20728 19990910.

PRIORITY: US 1998-99851 19980911; US 1999-136529 19990528.

AB The present invention provides an adenovirus comprising a recombinant fiber protein having modifications in the N-terminal, trimerization knob domain. A fiber incorporating such a protein exhibits reduced affinity for the native CAR protein substrate (cox sackievirus and adenovirus receptor) than does a wild-type adenoviral fiber trimer. Site-specific mutagenesis and competition expts. identified residues in the AB loop, B sheet, DE loop, and FG loop as important for CAR binding and conserved among adenoviral serotypes. An adenovirus serotype 5 mutant contg. a deletion in the FG loop (.DELTA.T489AYT492) was further modified by introducing the hemagglutinin (HA) epitope into the HI loop of the fiber knob (between amino acids 543 and 544). The result adenoviruses exhibit reduced binding capacity to CAR on std. HEK-293 cells due to the TAYT deletion; however, it binds with high affinity via its HA epitope to an anti-HA pseudoreceptor present on an anti-HA-293 cell line. Addnl. modifications may include the introduction of a high affinity RGD ligand. The present invention permits more efficient prodn. and construction of safer adenoviral vectors for gene transfer applications.

L93 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
1998:75999 Document No. 128:150383 Adenoviral-mediated cell targeting
commanded by the adenovirus penton base protein. **Wickham, Thomas
J.**; Kovesdi, Imre; Roelvink, Petrus W.; Brough, Douglas E.; McVey,
Duncan L.; Bruder, Joseph T. (Genvec, Inc., USA). U.S. US 5712136 A
19980127, 56 pp. Cont.-in-part of U.S. 5,559,099. (English). CODEN:
USXXAM. APPLICATION: US 1996-634060 19960417. PRIORITY: US 1994-303162
19940908.

AB A method of introducing an adenovirus into a cell comprises a particular
cell surface binding site as well as a chimeric adenovirus penton base
protein, and recombinant adenoviral vectors comprising the chimeric
adenovirus penton base protein for use in the method are provided. The
adenovirus is contacted with a bispecific mol. (antibody) comprising (1)

a
of component that selectively binds to a domain of the penton base protein
of the adenovirus, and (2) a second component that selectively binds the
particular cell surface site. Binding of the fiber protein of the
adenovirus to any cell surface mol. is abrogated (e.g., by the
introduction of a protease cleavage site), and the cell binds to a
specific site introduced into the penton base protein of the adenovirus.
The construction of chimeric adenovirus penton base protein and
recombinant adenoviral vectors is described.

L93 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3
1996:621434 Document No. 125:238646 Adenovirus gene therapy vectors using
fiber protein fusion proteins for efficient targetting of the virus.
Wickham, Thomas J.; Falck-Pedersen, Erik; Roelvink, Petrus W.;
Bruder, Joseph T.; Gall, Jason; Kovesdi, Imre (Genvec, Inc., USA; Cornell
Research Foundation, Inc.). PCT Int. Appl. WO 9626281 A1 19960829, 61

PP. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN,
CZ,
DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,
LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
SI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR,
IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN. (English). CODEN: PIXXD2.
APPLICATION: WO 1996-US1957 19960213. PRIORITY: US 1995-395381 19950221.

AB Adenovirus gene therapy vectors that have the receptor-binding domain of
the viral fiber protein substituted by a protein ligand for a specific
receptor and that carry a therapeutic gene are described. A series of
constructs in which the receptor binding domain of the adenovirus 5 fiber
protein is replaced with the corresponding domain of other adenovirus
fiber proteins or integrins is described. Use of the sialic acid-binding
domain of the adenovirus 3 fiber protein gives rise to a virus that will
bind to all known eukaryotic cell types. In vivo tests using a reporter
gene construct showed that partial substitution of the Ad5 fiber protein
with the Ad7 fiber protein did not affect infectivity of the virus.

=> log y

COST IN U.S. DOLLARS
FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
125.09	125.24

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

CA SUBSCRIBER PRICE

ENTRY

SESSION

-2.35

-2.35

STN INTERNATIONAL LOGOFF AT 10:19:45 ON 09 FEB 2001

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 16:36:35 ON 19 FEB 2001

L1 1204358 S VIRUS OR VIRION
L2 9 S NON-NATIVE LIGAND?
L3 0 S L1 AND L2
L4 264690 S LIGAND?
L5 1918 S HETEROLOGOUS AND L4
L6 138 S L5 AND L1
L7 1 S CD40 AND L6
L8 8752 S CD40
L9 4197 S L8 AND L4
L10 16 S L8 AND L5
L11 1 S L10 AND L1
L12 1188 S IMMUNE EFFECTOR CELL?
L13 0 S L12 AND L6
L14 0 S L12 AND L5
L15 1200364 S ANTIGEN?
L16 15434 S HETEROLOGOUS AND L15
L17 3431 S L16 AND L1
L18 58232 S ADENOVIR?
L19 118 S L17 AND 18
L20 7 S L5 AND RGD
L21 3 DUP REM L20 (4 DUPLICATES REMOVED)
L22 61995 S LIPOSOME
L23 4419 S L1 AND L22
L24 0 S L23 AND L5
L25 110 S L23 AND L4
L26 24 S L25 AND L15
L27 16 DUP REM L26 (8 DUPLICATES REMOVED)
L28 158 S ADENOVIR? CAPSID
L29 127 S L28 AND L1
L30 0 S NUCLEIC ACID VIRAL GENOME
L31 14655 S VIRAL GENOME
L32 202794 S NUCLEIC ACID?
L33 1672 S L31 AND L32
L34 0 S L33 AND L29
E ROELVINK/AU
E ROELVINK PETRUS/AU
E ROELVINK PETRUS OR P/AU
L35 0 S E4 AND LL5
E T WICKHAM/AU
E WICKHAM THOMAS/AU
L36 81 S E2 OR E3 AND L5
L37 8 S L36 AND L15
L38 6 DUP REM L37 (2 DUPLICATES REMOVED)
L39 0 S L36 AND L8
L40 0 S L39 AND L12
L41 0 S L36 AND L12
L42 24 S L26 AND L22
L43 16 DUP REM L42 (8 DUPLICATES REMOVED)